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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,618	02/22/2002	Alan D. Olstein	7005-0003	4458

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REED & EBERLE LLP
800 MENLO AVENUE, SUITE 210
MENLO PARK, CA 94025

EXAMINER

LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/082,618

Applicant(s)

OLSTEIN ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-72 is/are pending in the application.
- 4a) Of the above claim(s) 5, 10-63, 65 and 68-72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7-9, 64, 66 and 67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, subgroups A and 1, and the species wherein the transition metal is cobalt, in Paper No. 8 is acknowledged.
2. Claims 5, 10-63, 65, and 68-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

It is noted that the Applicant also stated "this election of species is for the sole purpose of the Examiner's initial search and examination, and that upon allowance of a generic claim, Applicant's are entitled to have all non-elected species encompassed by that claim examined. This statement is true in effect. Upon the determination that a generic claim is allowable, the Examiner will rejoin all claims within that claim. However, this will be done under USPTO linking claim practice. The Examiner has not made a species election requirement, but has indicated that the various groups of inventions are separate inventions falling within a common linking claim. Upon finding the linking claim allowable, it is assumed that the Examiner has determined that all inventions falling within the linking claim are allowable.

The Examiner agrees with the Applicant that claims 63 and 64 belong in Group I rather than in Group II. The restriction requirement is hereby so altered. The Examiner appreciates the oversight being brought to his attention.

Specification

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3. The disclosure is objected to because of the following informalities: on page 42, lines 25-26, the discussion of Example 3 refers to "the Nisin-Co (II) complex (of Example 3)." It appears that the Example referred to be the parenthetical should be Example 1.

Appropriate correction is required.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on May 28, 2002, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1-4, and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims read on chelated complexes of bacteriocins and a metal. The claims read on any such complexes, including both isolated complexes and complexes in the natural environment. However, it is known that at least some bacteriocin polypeptides bind to metals in nature, thereby forming the claimed chelated complexes. See e.g., Pommer et al., J Biol Chem 274(38): 27153-160. Because the claims read on complexes that may be found in nature, the claims read on non-statutory subject matter. It is noted that insertion of

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the term "isolated" to describe the complex in the claim will not satisfy this rejection because of the knowledge, and prior isolation, of such bacteriocins

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-4, 7, 8, 9, 64, 66, and 67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims read on complexes of bacteriocins, or fragments, homologs, and variants thereof (collectively-variants), with a transitional metal.

However, while the claims read broadly on the claimed complexes of transition metals with bacteriocin variants, the application does not provide and examples or other written description support for such variants. The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

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A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. In this case, the Applicant has not provided any such examples.

Nor has the Applicant provided any other means by which one of ordinary skill in the art could identify such variants. There is no disclosure of the sequences, regions, or motifs required in order for the claimed complexes to perform in the disclosed methods (i.e. those structural characteristics required for microbial binding or antibiotic effects). Because the Applicant has not provided any examples, or other means by which to identify bacteriocin variants that may be used in the claimed complexes, the Applicant has not provided adequate written description support for the full scope of the claimed invention.

9. Claims 1-4, 7, 8, 9, 64, 66, and 67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for complexes comprising a bacteriocin and a transition metal, does not reasonably provide enablement for complexes comprising bacteriocin variants and transition metals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims have been described above.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re

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Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

In the present case, the claims read expansively on complexes comprising any fragment, homologue, or variant of any bacteriocin. However, while the Applicant has provided general definitions of these terms in the specification (page 10), the application does not disclose any examples, or any other guidance to guide those in the art to such variants.

Bacteriocins are polypeptides. As such, the art surrounding the variation of these compositions is unpredictable. See e.g. Bowie et al., *Science* 247:1306-1310, at 1306 (indicating that while proteins tend to be tolerant of sequence substitution, the result of any particular substitution may have no effect, or may inactivate the protein). The reference teaches that there are several factors that determine the effect of a particular substitution on the function of a protein. E.g., the effect of the substitution on protein structure, and the participation of the substituted residue in the proteins activity. The Applicant has not provided any information as to what residues of the bacteriocins may be modified, or what regions of the peptides may be deleted, such that variants maintain the bacterial binding/antibiotic activities of the peptides.

In view of the breadth of the claims, the unpredictability of the art, and the absence of working examples or other guidance to those in the art towards operable embodiments of the

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claimed variant complexes, the application does not enable those skilled in the art to make or use complexes comprising any bacteriocin fragments, homologs, or variants.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-4, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Pommer et al., J Biol Chem, supra. The claims read on chelated complexes comprising a bacteriocin, and a transitional metal, including embodiments wherein the metal is Cobalt. Pommer discloses a bacteriocin that binds to the metals Zinc, Nickel, or Cobalt. Abstract. The reference further discloses that these complexes bind to and enter bacterium, including E. coli. Thus, the reference anticipates the identified claims.

Although the reference does not disclose that the metal bound to the protein may be used as a label in an assay, the functional language of the claims in this case demonstrate an intended use for the claimed composition. Intended uses do not, however, suffice to distinguish a claimed composition from a composition that meets a product claim's structural limitations. See e.g. MPEP § 2114. Because the protein taught by Pommer meets the structural limitations of the identified claims, it anticipates those claims even though it does not teach or suggest the intended use for the components of the claimed structure.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 1-4, 7, 8, 9, and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siddigi et al. (U.S. Patent 5,541,113), in view of Olstein et al., (U.S. Patent 5,750,357), and Timmer et al., EO 0659068. These claims read chelated complexes of bacteriocins, including lantibiotics, and the lantibiotic nisin, wherein the bacteriocin is complexed to a transitional metal, including cobalt.

Siddigi teaches methods for detecting analytes comprising attaching a transitional metal label to a ligand, and measuring the presence of the label to determine the presence of an analyte in a sample. Claims 1, and 22. Among the analytes that may be detected by this method are bacteria. Column 14, lines 9-125. The reference teaches that the "transition metal is preferably selected from Group 8 Periodic Table elements." Col. 12, lines 50-59. Among the Group 8 metals is Cobalt. See, Periodic Table, column 9. The selected label may then be chelated to a suitable organic ligand to the analyte. Id. It would therefore have been obvious to one of ordinary skill in the art to have used cobalt to as a label in the disclosed method. However, the reference does not teach the use of bacteriocins as ligands, and therefore does not teach the complexing of a bacteriocin to a transition metal.

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However, Olstein et al. teaches the use of chemically labeled antibiotics as ligands for the detection of pathogenic microorganisms. Col. 4, lines 15-33. The reference teaches the use of polymyxin, a bacterially produced antibiotic peptide, as the antimicrobial ligand. Column 1, lines 30-47, and column 2, lines 51-63. However, the reference does not teach the use of bacteriocins, lantibiotics, or nisin, as the antibiotic ligand.

The Timmer reference teaches that lantibiotics are a well known class of antibiotics, and that Nisin was one of the first such antibiotic to be discovered. Page 2, lines 37-45. Thus, because the reference teaches that Nisin is an antibiotic peptide, and because the Olstein reference teaches that such peptides are useful as ligand to pathogenic bacteria, it would have been obvious to those in the art to have used these peptides in the method described by Siddigi, and therefore to have made bacteriocin (nisin)/transitional metal (cobalt) complexes.

There would have been a reasonable expectation of success because the Olstein reference teaches that any antibiotic may be used as a bacterial ligand. Further, Meyer et al., (Arch Microbiol 167:67-77 at 74, of record in the IDS filed May 28, 2000) teaches that nisin and the other lantibiotics bind to the membranes of target cells, thus demonstrating that these peptides are pathogen ligands.

14. Claims 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siddigi, Olstein, and Timmer as applied to claims 1-4, 7, 8, 9, and 64 above, and further in view of Gasson et al., WO 96/16180. Claims 66 and 67 describe the method indicated above, wherein the bacteriocin has an amino acid sequence having either, respectively, a substitution, addition, or deletion of 1-3 residues from, or that is 90% homologous with, the sequence of SEQ ID NO: 5 of

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the application (disclosed as nisin precursor on page 17 of the application). The teachings of Siddigi, Olstein, and Timmer have been described above.

Gasson teaches the making and use of antibacterial variants of nisin. See e.g., pages 5-6. Because the reference teaches that such variants maintain the antibacterial activity of nisin, it would have been obvious to those in the art to have made such variants, and used them in the method described by Siddigi. The motivation to use the variants rather than the native form is the same as the reason for making the variants disclosed by Gasson: they may be produced with greater efficiency than the native form, and are thus more readily available for use in the described assays.

Conclusion

15. No claims are allowed.
16. The following prior art reference is made of record and is considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

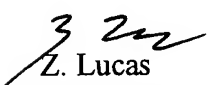
Isacson et al., *Analytica Chimica Acta*, 68: 339-62 (1974). This reference teaches the use of luminol, and its oxidants and transitions metal catalysts in detection assays. Further, the reference also teaches that luminol may be used in detection assays for microorganisms. Pages 356-57. However, the reference does not teach the use of the metal catalysts as labels for microbial ligands.


17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Z. Lucas
Patent Examiner
July 17, 2003


JAMES HOUSEL 7/28/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600